DETAILED ACTION

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/21/09 has been entered. Claims 15-23 are currently pending and under examination at this time. No claims have been amended, added, or canceled with the instant response. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in a previous office action.

Claim Rejections - 35 USC § 103

The rejection of claims 15-23 under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,849,452 (2/1/05), hereafter referred to as Zitvogel et al., in view of WO 01/85920 A2 (11/15/01), hereafter referred to as Banchereau et al., is maintained. Applicant's arguments have not been found persuasive in overcoming the rejection for reasons of record.

The applicant argues that Zitvogel et al. does not teach that contact between mature dendritic cells and NK cells results in NK cell proliferation. The applicant cites a passage from column 23 which discusses results from a working example and states that in that experiment

proliferation of NK cells was not observed. However, a description of the experiment discussed in column 23 starts in column 22 and clearly indicates that the experiment utilized immature dendritic cells, not mature dendritic cells, and speculates that the lack of proliferation may be due to culture conditions. As set forth in the rejection of record, Zitvogel et al. discloses that contact of mature dendritic cells with NK cells can result in the proliferation of at least a subset of NK cells (Zitvogel et al., columns 4 and 16). Nothing in Zitvogel et al., including the cited working example, calls this teaching into question. As such, applicant's argument is not found persuasive in overcoming the rejection of record.

Claims 15-23 are newly rejected under 35 U.S.C. 103(a) as being unpatentable of Ferlazzo et al. (2002) J. Exp. Med, Vol. 195(3), 343-351 in view of WO 01/85920 A2 (11/15/01), hereafter referred to as Banchereau et al.

Ferlazzo et al. teaches that the mature dendritic cells both activate and expand resting NK cells (Ferlazzo et al., pages 343-346, Figures 1 and 3). Specifically, Ferlazzo et al. teaches that culture of mature dendritic cells and resting NK cells induces NK cell proliferation and activation, as measured by ^{3}H-TdR incorporation, and by IFN-production and NK cell cytotoxicity assays (Ferlazzo et al., Figures 1 and 3). Ferlazzo et al. further teaches that the mature dendritic cells are produced from either whole blood or leukocyte concentrate by isolating dendritic cells precursors and incubating the cells in GM-CSF and IL-4 to produce immature dendritic cells, and maturing the immature dendritic cells in the presence of maturation inducing cytokines (Ferlazzo et al., page 344). Ferlazzo et al. also teaches the isolation of a purified population or a clonal population of NK cells by magnetic bead negative selection of

PBMC (Ferlazzo et al., page 344). Ferlazzo et al. also teaches contacting the NK cells activated by mature dendritic cells with antigen presenting allogeneic dendritic cells, where the antigen is the allogeneic MHC class I molecules (Ferlazzo et al., page 346).

Ferlazzo et al. differs from the instant invention by not teaching that the mature dendritic cells have been produced by contacting dendritic cell precursors with GM-CSF and IL-15. However, as noted above Ferlazzo et al. does teach that the mature dendritic cells can be produced by dendritic precursor cells with GM-CSF and IL-4, followed by maturation induction with cytokines (Ferlazzo et al., page 344). Banchereau et al. supplements Ferlazzo et al. by teaching that mature immunostimulatory dendritic cells can be produced by culturing dendritic cell precursors in the presence of GM-CSF and IL-15, and maturing the dendritic cells by treatment with LPS or CD40L (Banchereau et al., pages 8, 10, 12-13 and 19). Banchereau et al. further teaches that the mature dendritic cells produced from the culture of dendritic precursors in GM-CSF and IL-15 exhibited expression of CD1a, and high levels of CD80 and CD86 (Banchereau et al., page 13 and Figure 2a). Banchereau et al. also teaches exposing the dendritic cells to an antigen in the form of protein, peptides, or cells expressing the antigen (Banchereau et al., pages 11-13, and 25). Banchereau et al. further teaches that dendritic cells prepared with IL-15 and GM-CSF are similar in function to dendritic cells prepared with IL-4 and GM-CSF (Banchereau et al., page 22).

While Banchereau et al. did not do a direct comparison of the expression levels of CD1, CD80 and CD86 on dendritic cells produced from cultures in GM-CSF and IL-4, versus GM-CSF and IL-15, it is noted that the IL-15 dendritic cells of Banchereau et al. were produced using the same culture conditions, i.e. culture in IL-15 and GM-CSF, and appear to express the same

markers as the cells recited in the instant methods. "When the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent." See MPEP 2112.01 or *In re Best*, 195 USPQ 430, 433 (CCPA 1997). Further, the applicant is reminded that the office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 USPQ 1302, 1303 (BPAI 1993), *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2d 1922, 1923 (BPAI 1989).

Therefore, in view of the similarities in function between mature dendritic cells produced from cultures of dendritic precursor cells exposed to IL-15 and GM-CSF and those produced from cultures of dendritic precursor cells exposed to IL-4 and GM-CSF as taught by Banchereau et al., it would have been *prima facie* obvious to the skilled artisan at the time of filing to substitute the mature dendritic cells produced from cultures of dendritic precursor cells exposed to IL-15 and GM-CSF taught by Banchereau for the mature dendritic cells produced from cultures of dendritic precursor cells exposed to IL-4 and GM-CSF in the methods of activating and expanding NK cells taught by Ferlazzo et al. with a reasonable expectation of success that such a substitution would be capable of inducing the activation and proliferation of NK cells in tissue culture.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, the technology center fax number is (571) 273-8300. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

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